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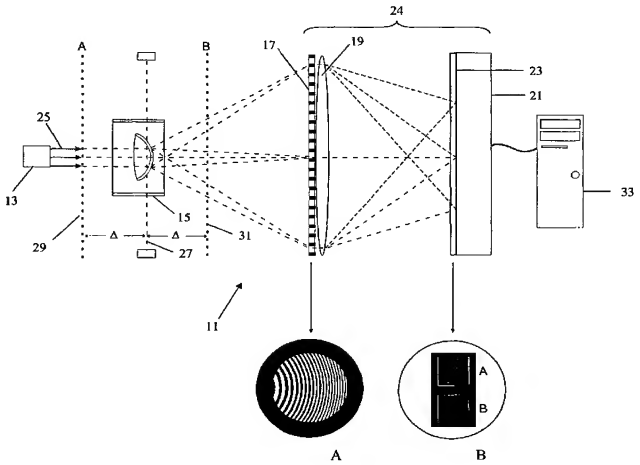

(57) Abstract: Apparatus (11) for determining if a cornea (whether in vitro or in vivo) has been modified (either surgically or otherwise). The method includes the steps of: passing a beam of collimated light (13) a (either coherent or incoherent) through the cornea to produce a distorted wavefront; determining the characteristics of the distorted wavefront; and analyzing the distorted wavefront for characteristics that identify the presence of a modification. The analysis of the distorted wavefront can be for the presence of higher order aberrations, or Gausian characteristics which are indicative of modifications. More particularly, the method includes the steps of providing an optical system that has a pupil plane and an image plane at a detector; positioning the cornea in the pupil plane; passing a collimated beam of light through the cornea to produce at least two images in the image plane; determining the characteristics of the distorted wavefront; and analyzing the distorted wavefront for characteristics that identify the presence of a modification.

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HOLDER FOR CORNEAS

Field of the Invention

[0001] This invention relates to cornea holders for use in wavefront sensing to determine whether or not a cornea has been altered (due to corrective surgery, or accident).

Background of the Invention

[0002] In the United States about 40,000 corneal transplant operations are performed each year. While success of such surgery may depend upon a number of other factors, one factor that always has an effect on the outcome is the condition of the donor cornea. In the United States, a donor cornea must be transplanted within 7 days of harvesting. Outside the United States donor corneas may be used up to 14 days after harvesting. Additionally, it is essential to use only corneas which have not been modified (e.g., the subject of photorefractive surgery).

[0003] The growth of refractive surgery over the last five years has been dramatic. In the August 2000 issue of Archives of Ophthalmology, P.J. McDonnell, M.D. states that this year alone over 1,500,000 refractive procedures will be performed. As beneficial as these procedures are, the individual corneas are permanently altered, which makes them unsuitable for corneal transplanting.

[0004] The increase in refraction surgery increases the likelihood that a modified cornea will be harvested for transplant purposes. Unfortunately, it is generally not possible to conclusively tell, either visually or under a microscope, whether such a donor cornea has been subjected to a surgical procedure or otherwise altered.

[0005] Even when properly stored in a container (e.g., a Chiron Ophtholmics cornea container) filled with Optisol ® or another appropriate solution, a donated cornea changes optically in the 14 day time period referenced above. The interior starts to develop optical scatter sources and the optical power of the cornea changes. The scatter resources manifest themselves as randomly distributed optical aberrations which increase over time. It is believed that this is caused by the cells of the harvested cornea not being able to reject waste material. The change in optical power is believed to be caused by an overall relaxation of the tissue. Regardless of the cause, the net result is that these aberrations produce scintillation and static aberrations when a beam of light is passed through a donated cornea.

[0006] PCT/GB99/00658 (International Publication No. WO 99/467768), based on applications filed in Great Britain on March 10, 1998 and December 23, 1998, discloses a three dimensional imaging system including a lens and a distorted diffraction grating which images objects located at different distances from the grating

simultaneously and spatially separated in a single image plane. The grating is distorted according to a quadratic function so as to cause the images to be formed under different focus conditions. It is stated that the system is useful for simultaneously imaging multiple layers within a three dimensional object field, and has applicability in a number of fields including optical information storage, imaging short-time scale phenomena, microscopy, imaging three dimensional object structures, passive ranging, laser beam profiling, wavefront analysis, and millimeter wave optics. The ability to make wavefront measurements is not disclosed or claimed.

[0007] P.M. Blanchard et al., "Multi-Plane Imaging With a Distorted Grating," Proceedings of the 2nd International Workshop on Adaptive Optics for Industry and Medicine, World Scientific, pp. 296-301, 12-16 July 1999, describe a technique for simultaneously imaging multiple layers within an object field onto the detector plane of a single detector. The authors, who are the named inventors in PCT/GB99/00658, state that the imaging of multiple layers within an object field is "useful in many applications including microscopy, medical imaging and data storage." (See page 296.) The apparatus includes the use of a binary diffraction grating in which the lines are distorted such at each different level of defocus is associated with each diffraction order. When such a grating is placed in close proximity to a lens, the grating creates multiple foci of the image. This multi-foci effect enables the imaging of multiple object planes onto a single image plane.

[0008] L. J. Otten et al. "3-D Cataract Imaging System," Proceedings of the 2nd International Workshop in Adaptive Optics for Industry and Medicine, World Scientific, pp. 51-56, describe optics and an associated diagnostic system for volumetric, in vivo imaging of the human lens to characterize or grade cataracts. The described method and apparatus are based on the use of a distorted grating (of the type disclosed in PCT/GB99/00658 and the Blanchard et al. paper, supra) in conjunction with a focusing lens and a re-imaging lens. (See Figure 1 of this reference.) The quadratic phase shift, introduced by the grating, leads to a different degree of defocus in all diffraction orders, which produces a series of images of different layers of the cataract, each with different defocus conditions, simultaneously and side-by-side on the detector. Thus, in-focus images of different object planes are produced.

[0009] Analysis of the optical images referenced above requires the use of the Intensity Transport Equation (I.T.E.) and the employment of a Green's function to produce a wavefront map. S. Woods, P.M. Blanchard and A.H. Greenaway, "Laser Wavefront Sensing Using the Intensity Transport Equation," Proceedings of the 2nd International Workshop on Adaptive Optics for Industry and Medicine, World Scientific, pp. 260-265, 12 - 16 July 1999, describe both the I.T.E. and a Green's function solution thereto in conjunction with laser wavefront sensing.

Objects of the Invention

[0010] It is an object of the present invention to provide a holder for a donor cornea which does not mask optical data from such cornea.

[0011] It is another object of the present invention to provide a holder for a donor cornea that has optical windows that are substantially free of distortion which would mask corneal optical data.

[0012] It is still another object of the present invention in which the optical windows have less than $\lambda/10$ distortions.

[0013] These and other objects will be apparent from the description which follows.

Summary of the Invention

[0014] A method of determining if a cornea (whether in vitro or in vivo) has been modified (either surgically or otherwise). The method includes the steps of: passing a beam of collimated light a (either coherent or incoherent) through the cornea to produce a distorted wavefront; determining the characteristics of the distorted wavefront; and analyzing the distorted wavefront for characteristics that identify the presence of a modification. The analysis of the distorted wavefront can be for the presence of higher order aberrations, or Gausian characteristics which are indicative of modifications. More particularly, the method includes the steps of providing an optical system that has a pupil plane and an image plane at a detector; positioning the cornea in the pupil plane; passing a collimated beam of light through the cornea to produce at least two images in the image plane; determining the characteristics of the distorted wavefront; and analyzing the distorted wavefront for characteristics that identify the presence of a modification.

[0015] The apparatus for determining whether a cornea has been surgically modified includes: a source of collimated light, an optical system including a distorted grating and an imaging lens (which have a pupil plane, first and second virtual planes, and an image plane); structure for positioning the cornea in the pupil plane; means for recording the images of the first and second virtual planes; means for determining from the first and second images the distorted wavefront; and means for analyzing said wavefront for characteristics indicative of modified corneas. The first and second virtual planes are on opposite sides of and equally spaced from said pupil plane.

[0016] The structure for positioning the cornea (which is immersed in a suitable storage fluid) is a container which includes: a housing having first and second ends; structure positioned within the housing for supporting the perimeter of the cornea; a first plano/plano lens for closing the first end of the housing; and a cap for closing the second end of the housing. The cornea support is substantially symmetrical with respect to an optical axis. The first plano/plano lens is substantially perpendicular to the optical axis. Finally, the cap includes a second plano/plano lens which is substantially parallel to the first plano lens. The first and second plano/plano lens, which are substantially centered with respect to the axis, have less than $\lambda/10$ total

distortions. The support structure includes a cage and a pedestal with the cage being supported by the pedestal. Preferably, the cage and pedestal are integrally formed with the housing. Finally, the cap has a top portion and a skirt which axially inwardly spaces the second lens from the top portion to create an annular area where air will collect when the container is holding a cornea and fluid, so that air will not interfere with a beam of light passing through the first and second plano/plano lenses and cornea.

Brief Description of the Drawings

[0017] Figure 1 is a schematic of the optical system of the instrument to characterize donor corneas;

[0018] Figure 1A is the front view of the distorted grating used in the instrumentation to characterize corneas;

[0019] Figure 1B is the front view of the detector plane of the detector of the instrumentation to characterize corneas, and the images in such plane;

[0020] Figure 2 is a cross-section view of an optical cornea container of the present invention;

[0021] Figure 3 is a cross-sectional, perspective view of an improved cornea container of the present invention;

[0022] Figure 4 is a cross-sectional view of the improved optical cornea container of Figure 3 in the open position;

[0023] Figure 4A is a cross sectional view of the improved optical cornea container of Figure 3 in the closed position.

[0024] Figure 5 is a diagram showing the baseline date of the system of Figure 1, with no cornea or container;

[0025] Figure 6 is a diagram showing the baseline date of the system of Figure 1, with the container of Figure 2 filled with Optisol®, but with no cornea;

[0026] Figure 7 is a diagram showing the data from an unmodified cornea L, held in the container of Figure 2, positioned in the pupil plane of Figure 1, and exposed to coherent and collimated light;

[0027] Figure 8 is a diagram showing the data from a an unmodified cornea R, held in the container of Figure 2, positioned in the pupil plane of Figure 1, and exposed to coherent and collimated light;

[0028] Figure 9 is a diagram showing the data from cornea L after it has been surgically modified, again held in the container of Figure 2, positioned in the pupil plane of the system of Figure 1, and exposed to the same coherent and collimated light;

[0029] Figure 10 is a diagram showing the data from the cornea R after it has been surgically modified, again held in the container of Figure 2, positioned in the pupil plane of Figure 1, and exposed to the same coherent and collimated light;

[0030] Figure 11 is a three dimensional presentation of the data set forth in Figure 7;

[0031] Figure 12 is a three dimensional presentation of the data set forth in Figure 8;

[0032] Figure 13 is a three dimensional presentation of the data set forth in Figure 9;

[0033] Figure 14 is a three dimensional presentation of the data set forth in Figure 10;

[0034] Figure 15 is a three dimensional presentation of the wavefront of cornea LL which was modified by a LASIK procedure (prior to the death of the donor), held in the container of Figure 2, positioned in the pupil plane of Figure 1, and exposed to coherent, illuminated light;

[0035] Figure 16 is a three dimensional presentation of the wavefront of cornea LR which was modified by a LASIK procedure (prior to the death of the donor), held in the container of Figure 2, positioned in the pupil plane of Figure 1, and exposed to coherent, illuminated light; and

[0036] Figure 17 is a schematic of the optical system used to characterize in vivo corneas.

Description of the Preferred Embodiment

[0037] With reference to Figure 1, the apparatus 11 for determining whether an in vitro cornea has been modified (either surgically or otherwise) includes a source of collimated coherent light 13, a cornea container 15, a distorted diffraction grating 17, a high quality imaging lens (or lens set) 19, and a detector 21 (either film or electronic) having a detector plane 23. (Grating 17, lens 19 and detector 21 are sometimes referred to as wavefront sensor 24.) Apparatus 11 also includes a beam path 25, a pupil plane 27, first virtual plane 29, second virtual plane 31, and a computer 33. Computer 33 is connected to detector 21, via a data acquisition device such as a frame grabber (located within the computer housing). Computer 33 stores the images form detector 21, determines the wavefront from the stored images, and analyzes the wavefront for characteristics that identify an altered cornea (e.g. compares the wavefronts to a stored norm). The representation of the virtual planes between source 13 and sensor 24 is for convenience only. In the preferred embodiment they are 73 cm on either side of pupil plane 27. Source 13 is a coherent laser such as a 633 nm HeNe laser. As those skilled in the art will appreciate non-coherent sources, such as spectrally band filtered white light, could also be used.

[0038] With grating 17 in close proximity to lens 19 (typically these two elements would, in fact, be in contact with each other along beam path 25), the 0, +1 and −1 diffraction orders of grating 17 image pupil plane 27, virtual object plane 29 and virtual object plane 31 are projected onto detector plane 23. The higher order diffraction orders are cut off by an appropriately placed field stop so as not to contaminate the image of the 0 and +1 and −1 orders. Further, with the zero order being an image of the pupil plane 27, the images in the +1 and −1 diffraction orders correspond to virtual image planes equidistant from and an opposite sides of pupil plane 27. The grating is distorted according to,

$$\Delta_x(x,y) \approx \frac{W_{20}d}{\lambda R^2}\left(x^2+y^2\right)$$

where λ is the optical wavelength, x and y are Cartesian co-ordinates with an origin on the optical axis and R is the radius of the grating aperature which is centered on the

optical axis. The parameter W_{20}, defines the defocusing power of the gratings, and is the standard coefficient of the defocus equivalent on the extra pathlength introduced at the edge of the aperature, in this case for the wavefront diffracted into the +1 order. The phase change ($\varnothing_m$) imposed on the wavefront diffracted into each order m is given by,

$$\varphi_m(x,y) = m\frac{2\pi W_{20}}{\lambda R^2}\left(x^2+y^2\right)$$

[0039] The various containers in which donor corneas are stored are unusable for optical diagnostics. The aberrations produced by the walls of such containers mask the aberrations exhibited by corneas both unaltered and altered. With reference to Figure 2, optical cornea container 15 includes cylindrical housing 41, first optical window 43, second optical window 45, and fluid containment ring 47. Housing 41 and ring 47 are concentric rings, both bonded to optical window 43. Window 43 is a plano/plano lens having surfaces 49, 51 which are substantially concentric with respect to beam path 25 and substantially perpendicular thereto. Similarly, window 45 is a plano/plano lens having surfaces 53, 55 which are also substantially concentric with and substantially perpendicular to beam path 25. Collectively, windows 43 and 45, including surfaces 49, 51 and 53, 55 have total aberrations of less than $\lambda/10$. In operation, cavity 57 is filled with Optisol®, or another solution suitable for the storage of donor corneas, to the top of housing 41 so that the meniscus causes such fluid to slightly over fill cavity 57. Window 45 is then slid over housing 41 without trapping any air in cavity 57. Excess fluid is collected between housing 41 and ring 47.

[0040] With reference to Figures 3 and 4, improved cornea container 15^1 includes a cylindrical body portion 61, a cornea support cage portion 63, and a cap portion 65. Body portion includes a bottom surface 67, an upper skirt portion 69 having a groove 71 therein for supporting an o-ring seal 73 and threads (not shown), and a cavity 74. Body portion 61 also includes a conical shaped skirt 75 integral with bottom surface 67 for centrally positioning cage portion 63 within body portion 61 as illustrated in Figures 3 and 4. Cage portion 63 includes a plurality of fingers 77, which are supported by ring portion 79 of skirt 75 in a cylindrical pattern concentric

with axis 81. As best illustrated in Figure 4, the free ends of fingers 77 include, inter alia, an inwardly sloping bevel 83 and notch 84 for supporting a donor cornea, such as illustrated at 85. Finally, body portion 61 includes a plano/plano lens 87 secured to ring portion 79. Lens 87 has parallel plano surfaces 89 and 91 which are substantially centered with respect to axis 81 and substantially perpendicular thereto. Cap portion 65 includes a skirt portion 93, a shoulder 95 which seats against 73, a top portion 96, and an inner skirt portion 97 having a circumferential lip 99. Inner surface 100 includes threads (not shown) which mate with the threads (also not shown) on skirt 69. Secured to lip 99 is a second plano/plano lens 101 having plano parallel surfaces 103and 105. When cornea container 15^1 is closed, with seal 73 received in circumferential recess 95, surfaces 103 and 105 are substantially centered with respect to axis 81 and substantially perpendicular thereto. Collectively, the aberrations in lenses 87 and 101, including surfaces 89, 91, 103 and 105, have a total aberration of less than $\lambda/10$.

[0041] In operation, donor cornea 85 is placed in cage 63, with a portion of the convex surface thereof in contact with bevels 83 and the perimeter received within notches 84. In this position, donor cornea is substantially centered about axis 81. Cavity 74 is then filled with a suitable storage fluid and capped by screwing on cap 65. As can be seen from Figure 4A, because inner skirt portion 97 projects inwardly, closure of cap 65 will force excess fluid out of cavity 74. In the event that there is any under filling of cavity 74, any air which might be trapped in cavity 74 is collected in annular area 107 (outside of the beam path).

[0042] With nothing in pupil plane 27 of apparatus 11 (e.g., cornea container 15 removed) and source 13 present, the images recorded on detector plane 23 are as illustrated in Figure 1B. Data was collected without any disturbances (i.e., no cornea container, cornea storage solution, or cornea) to determine the residual errors in the optics and, thus, establish the base line for instrument 11. With reference to Figure 5, the raw images as recorded by detector 21 are shown along with the reduced Zernike terms, annotated to show where the various types of data are located in the figure. All the data are taken using a 633 nanometer HeNe laser as the illumination source. Most of the error is tip and tilt, which is the result of not accurately aligning wavefront sensor 24 and for not accurately accounting for where the distorted grating images

were actually placed on detector plane 23. These two terms can be made equal to zero by: (1) subtracting them in the analysis of the wavefront to accommodate images that are not exactly centered on the same line; or (2) a more precise alignment of wavefront sensor 24. The other aberrations (e.g. focus) are seen to be small, on the order of or less than 0.1λ. All the baseline aberrations, including tip and tilt, can be subtracted from the cornea data.

[0043] Next, a baseline for optical system11, with cornea container 15 located in pupil plane 27 and cavity 57 filled with Optisol® solution, but without a cornea, was established. The baseline data is set forth in Figure 6. Again, all aberrations can be compensated for or eliminated using the criteria set forth above with regard to Figure 5.

[0044] After establishing the baseline, an unmodified donor cornea L was placed in cornea container 15, centered as illustrated in Figure 2, filled with Optisol® solution, and then closed with optical window 45 in the manner set forth above. Container 15 was then placed in instrument 11, in optical beam path 25 and with cornea L in pupil plane 27, as illustrated in Figure 1. If necessary, predetermined aberrations can be introduced into the beam path prior to the beam reaching the pupil plane and subsequently accommodated in the analysis of the data. The measured errors are illustrated in Figure 7. In this figure the tip and tilt terms are irrelevant since they are associated with cornea container 15 and, the orientation of cornea L therein. Cornea L is seen to have focus and astigmatism errors.

[0045] As with cornea L, cornea R was placed in container 15, and centered as set forth above. Cavity 57 as was then filled with Optisol® and closed with optical window 45. Cornea container 15 was then placed in the pupil plane of instrument 11. The measured errors are illustrated in Figure 8. As with cornea L, the tip and tilt terms for cornea R are irrelevant since they are associated with container 15 and the specific orientation of cornea R therein, both of which are not controlled. As is evident from Figure 8, cornea R has focus, astigmatism and coma errors.

[0046] The data illustrated in Figures 7 and 8 were collected using a 12mm diameter collimated beam. The measurements were repeated with an 8 mm, and 5 mm collimated beams to see if the measured aberrations were being effected by the irregular outer edge of the corneas. The effect of reducing the beam size was to

improve the quality of the images but at the expense of brightness and the area examined. All data were collected with the beam centered on the cornea.

[0047] To demonstrate the ability of apparatus 11 to detect surgically modified corneas, cornea L was then modified using a PRK procedure to add 4 diopters of focus change. Cornea R was also subjected to the same procedure to add 8 diopters of focus change. After modification each cornea was, in turn, again centered in cavity 57, which was filled with Optisol® and closed, and container 15 placed in apparatus 11 with the modified cornea again in pupil plane 27.

[0048] The measured errors for cornea L (modified) are illustrated in Figure 9. Again, tip and tilt are irrelevant since they are associated with cornea container 15 and the orientation of cornea L (modified) therein. Cornea L (modified) is seen to have considerably larger focus and astymatism errors then cornea L. The higher order errors (coma 1, coma 2, trifoil 1, trifoil 2 and spherical) are also considerably larger and provide one of the basis for the determination that the cornea has been altered.

[0049] The measured errors for cornea R (modified) are illustrated in Figure 10. As before, tip and tilt are irrelevant. Cornea R (modified) is seen to have considerably larger focus and astymatism errors than cornea R. As with cornea L (modified) the higher order aberrations have also increased (again indicating that the cornea has been modified). A summary of the results is shown in Table 1. Note that the measured difference (in waves) between the two corneas is a factor of 2, the same amount of focus difference introduced by the PRK procedure.

Table 1

Cornea	Focus Term Before Modification (waves)	Focus Term After Modification (waves)	Difference (waves)
L	1.77	3.23	1.46
R	1.024	4.132	3.108

[0050] An alternative way of illustrating the data set forth in conjunction with Figures 7-10 is to present the distorted wavefronts produced by the respective unaltered and altered corneas as three dimensional images. This type of presentation is illustrated in Figures 11-14, wherein: Figure 11 corresponds to Figure 7; Figure 12, to Figure 8; Figure 13, to Figure 9; and Figure 14, to Figure 10. In Figures 11-16, the

grey scale on the right is a representation of the distortion. Note the similarities of the Gaussian-like slope of the wavefront aberrations measured for the modified corneas, which provides another basis for determining whether a cornea has been modified.

[0051] Right (RL) and left (LL) corneas from a donor who had the LASIK corrective surgery prior to death were measured in the same manner as the unmodified corneas L and R (Figures 7 and 8) and the PRK modified corneas (Figures 9 and 10). Figure 15 is the left (LL) LASIK modified cornea. Figure 16 is the right (RL) LASIK modified cornea. The characteristic Gausian-like shape of the wavefront produced by the laser surgery is clearly present in both corneas. As with the PRK modified corneas (Figures 9 and 10), the higher order aberrations are considerably larger than those aberrations in the unmodified corneas (Figure 7 and 8).

[0052] The basis for extracting the wavefront from the data collected from detector 21 is to solve the Intensity Transport Equation (I.T.E.). The I.T.E. is derived by expressing the parabolic wave equation for complex amplitude in terms of intensity (*I*) and phase (Ø), and relates to the rate of change of intensity in the direction of the propagation to the transverse gradient and La Placian of the phase:

$$-\frac{2\pi}{\lambda}\frac{\partial I}{\partial z} = I\nabla^2\varphi + \nabla I \cdot \nabla\phi$$

For a uniformly illuminate aperture, *R,*, with perimeter *P*, the ITE simplifies to

$$\frac{2\pi}{\lambda}\frac{1}{I_o}\frac{\partial I}{\partial z} = W_R\,\nabla^2\varphi - \delta_P\frac{\partial\phi}{\partial\eta}$$

where W_R is the aperture function (= 1 inside *R, = 0 outside R)*, δ_p is a delta-function around *P*, and $\partial\phi / \partial\eta$ is the normal derivative of Ø on *P*.

[0053] Consider the problem of finding the phase at a particular point **r**. We can express this in terms of an integral involving a delta-function as follows:

$$\phi(\mathrm{r}) = \int_R \phi(\mathrm{r}')\delta(\mathrm{r}-\mathrm{r}')$$

If we have a Green's function satisfying

$$\nabla^2 G(\mathrm{r},\mathrm{r}') = \delta(\mathrm{r}-\mathrm{r}'), \frac{\partial G(\mathrm{r},\mathrm{r}')}{\partial \eta}\Big|_P = 0$$

then we can say

$$\phi(\mathrm{r}) = \int_R \phi(\mathrm{r}')\nabla^2 G(\mathrm{r},\mathrm{r}')$$

Applying Green's 2nd identify;

$$\phi(\mathrm{r}) = \int_R G(\mathrm{r},\mathrm{r}')\nabla^2\phi(\mathrm{r}') + \oint_P \phi(\mathrm{r}')\frac{\partial G(\mathrm{r},\mathrm{r}')}{\partial \eta} - \oint_P G(\mathrm{r},\mathrm{r}')\frac{\partial \phi(\mathrm{r}')}{\partial \eta}$$

and the boundary condition on the Green's function;

$$\phi(\mathrm{r}) = \int_R G(\mathrm{r},\mathrm{r}')\nabla^2\phi(\mathrm{r}') - \oint_P G(\mathrm{r},\mathrm{r}')\frac{\partial \phi(\mathrm{r}')}{\partial \eta}$$

$$= \int_R G(\mathrm{r},\mathrm{r}')\left(\nabla^2\phi(\mathrm{r}') - \delta_P\frac{\partial \phi(r')}{\partial \eta}\right)$$

we get the solution. The term in parenthesis is the right hand side of the ITE. The wavefront phase is thus obtained by measuring the intensity derivative (the left hand side of the ITE), multiplying by the Green's function and integrating;

$$\phi(\mathrm{r}) = -\frac{2\pi}{\lambda}\frac{1}{Io}\int_R G(\mathrm{r},\mathrm{r}')\frac{\partial I(r')}{\partial \mathrm{z}}$$

The intensity derivative,

$$\frac{\partial I(\mathrm{r}')}{\partial \mathrm{z}}$$

is obtained by the subtraction of two pixellated images. The Green's function is be pre-calculated on the appropriate grid and the solution obtained by the matrix multiplication:

$$\phi = -\frac{2\pi}{\lambda}\frac{1}{I_o}\sum_J Gi_j\left(\frac{\partial \mathrm{I}}{\partial z}\right)_j$$

[0054] The particular solution will vary, depending on the specifics of the optical design, the detector and the distorted grating used.

[0055] While the foregoing has dealt with donor corneas, the same basic procedure can also be used on in vivo corneas. With reference to Figure 17, system 111 includes a source of collimated coherent light 113, a beam splitter 115, a distorted diffraction grating 117, a high quality imaging lens or lens set 119, and a detector 121 (either film or electronic) having a detector plane 123. As with instrument 11, grating 117, lens 119 and detector 121 constitute wavefront sensor 124. System 111 also includes a beam path 125, a pupil plane 127, a first virtual plane 129, a second virtual plane 131, and a computer 133 connected to detector 121 by a data acquisition device, such as a frame grabber located within the computer housing. As with the first embodiment, source 113 is a coherent laser whose energy, when projected into the eye, meets FDA approved eye safe levels. Grating 117, which is also distorted according to the grating equation set forth above, is in close proximity with or touching lens 119. System 111 also includes apparatus, not shown, for positioning the patient's head such that his/her cornea is in pupil plane 127.

[0056] In operation the beam from source 113 is directed through beam splitter 115, through the cornea 135 and of eye 137, onto the retina 139 where it is reflected back through the cornea and then directed, by beam splitter 115 to wavefront sensor 124. As with instrument 11, the 0, +1 and –1 diffraction orders of grating 117 image pupil plane 127, virtual object plane 129 and virtual object plane 131 onto detector plane 123. Again, the higher order diffraction orders are cut off by an appropriately placed field stop so as not to contaminate the image of the 0 and +1 and –1 orders. Further, with zero order being an image of the pupil plane 127, the images in the +1 and –1 diffraction orders correspond to virtual image planes equidistant from and opposite sides of pupil plane 127. Computer 133 stores the images from detector 121, determines the wavefront from the stored images in the manner set forth above with the I.T.E. and a Green's function, and then analyzes the wavefront for the characteristics that identify an altered cornea (e.g., compares the wavefront to a stored norm).

[0057] Whereas the drawings and accompanying description have shown and described the preferred embodiment of the present invention, it should be apparent to those skilled in the art that various changes may be made in the form of the invention without affecting the scope thereof.

I Claim

1. A container for holding a donor cornea and a fluid suitable for storing a cornea, said container comprising:
   a. a housing having first and second ends;
   b. means, positioned within said housing, for supporting said perimeter of said cornea;
   c. a first plano/plano lens for closing said first end of said housing, said first plano/plano lens being substantially perpendicular to said optical axis; and
   d. a cap for closing said second end of said housing, said cap including a second plano/plano lens, said second plano/plano lens being substantially parallel to said first plano/plano lens.
2. The container of claim 1, wherein said first and second plano/plano lens have less than $\lambda/10$ total distortions.
3. The container of claim 1, further including a seal, position between said housing and said cap.
4. The container of claim 1, wherein said means for supporting said cornea includes a cage and a means for supporting said cage.
5. The container of claim 1, wherein said first and second plano/plano lenses are substantially centered with respect to said axis.
6. The container of claim 1, wherein said cap has a top portion and a skirt, said second plano/plano lens having a perimeter, said perimeter being radially inwardly spaced from said skirt and axially inwardly spaced from said top portion to create an annular area where air will collect when said container is holding a cornea and said fluid, so said air will not interfere with a beam of light passing through said first and second plano/plano lenses.

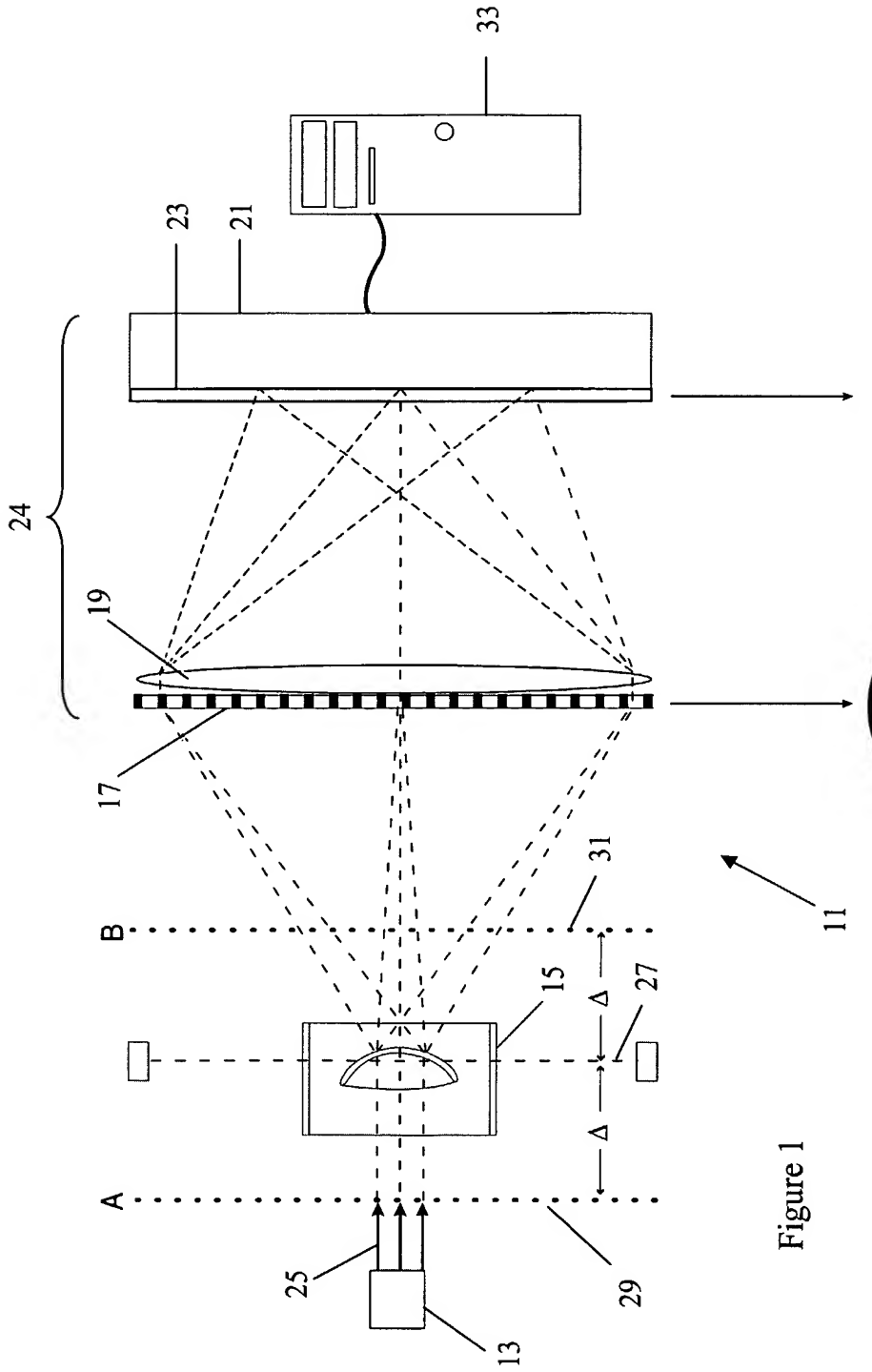


Figure 1

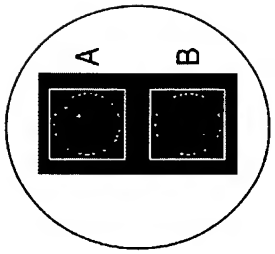


Figure 1B

Figure 1A

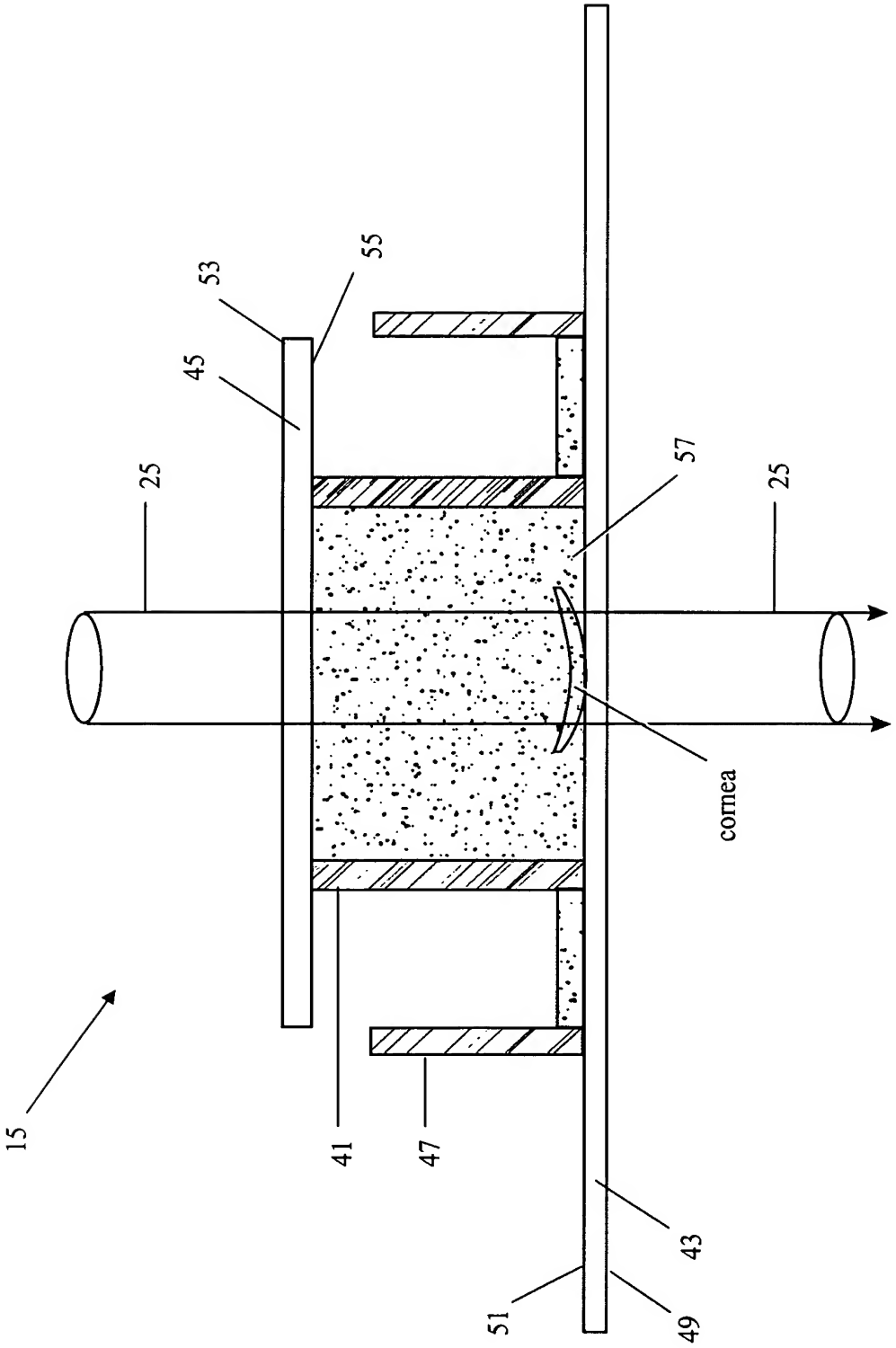


Figure 2

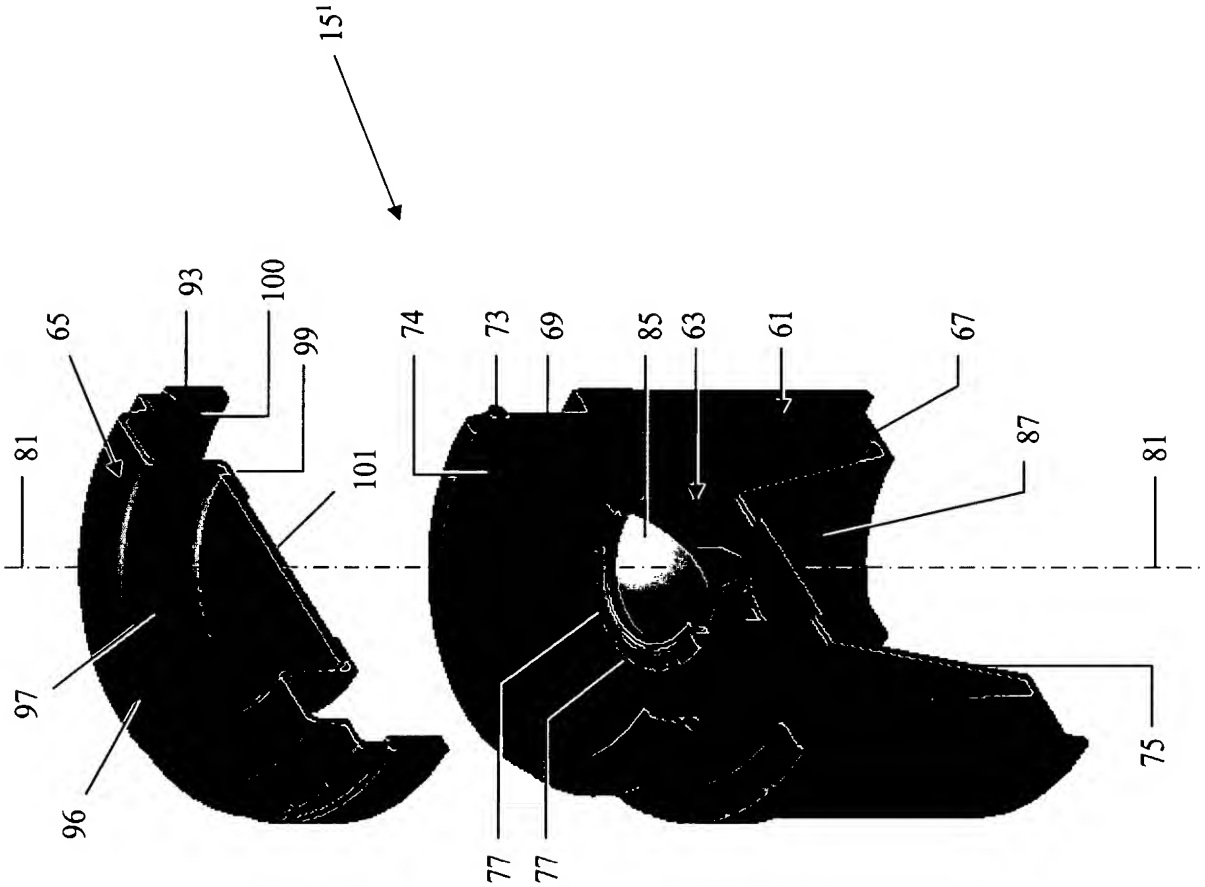
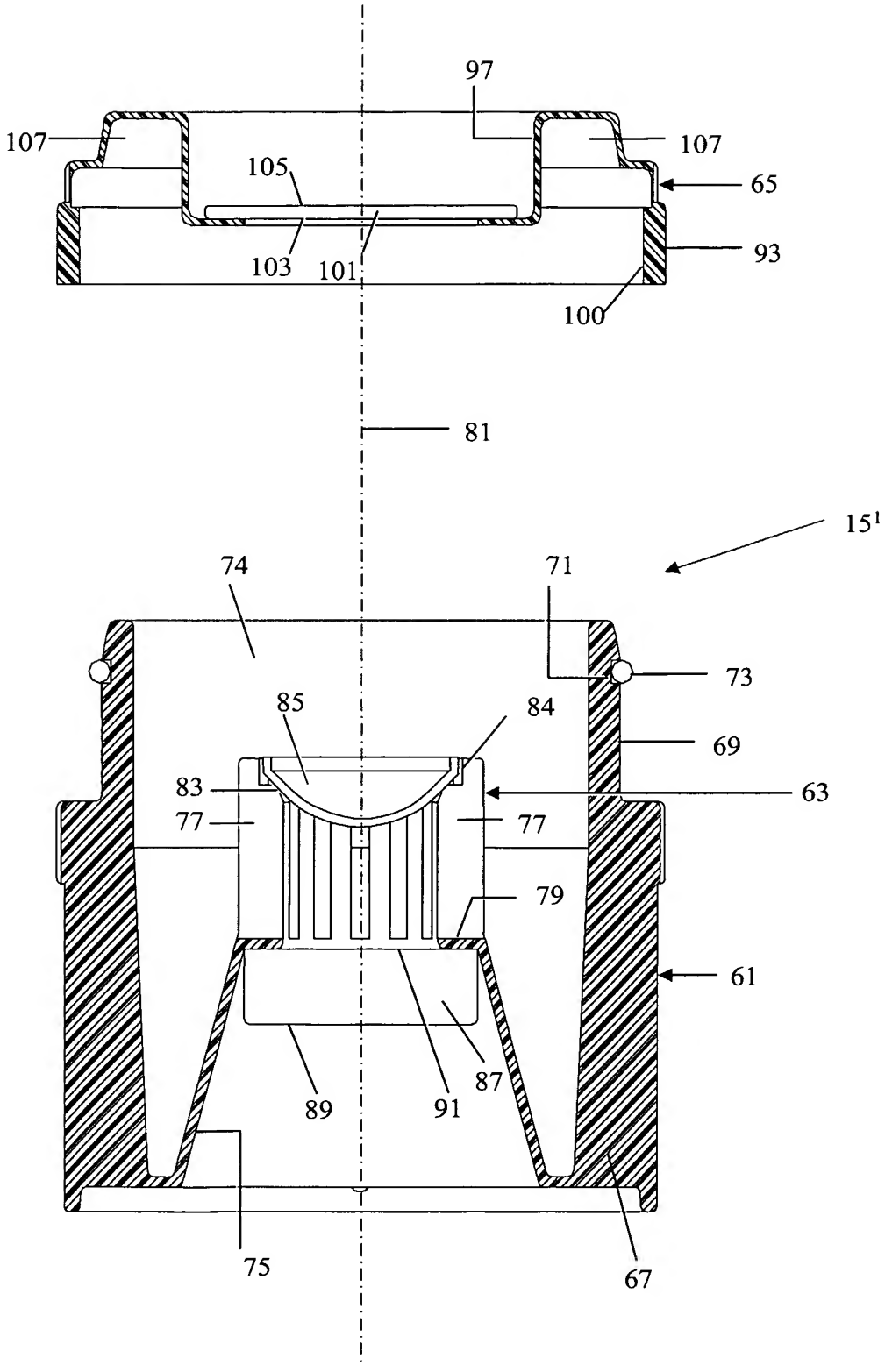


Figure 3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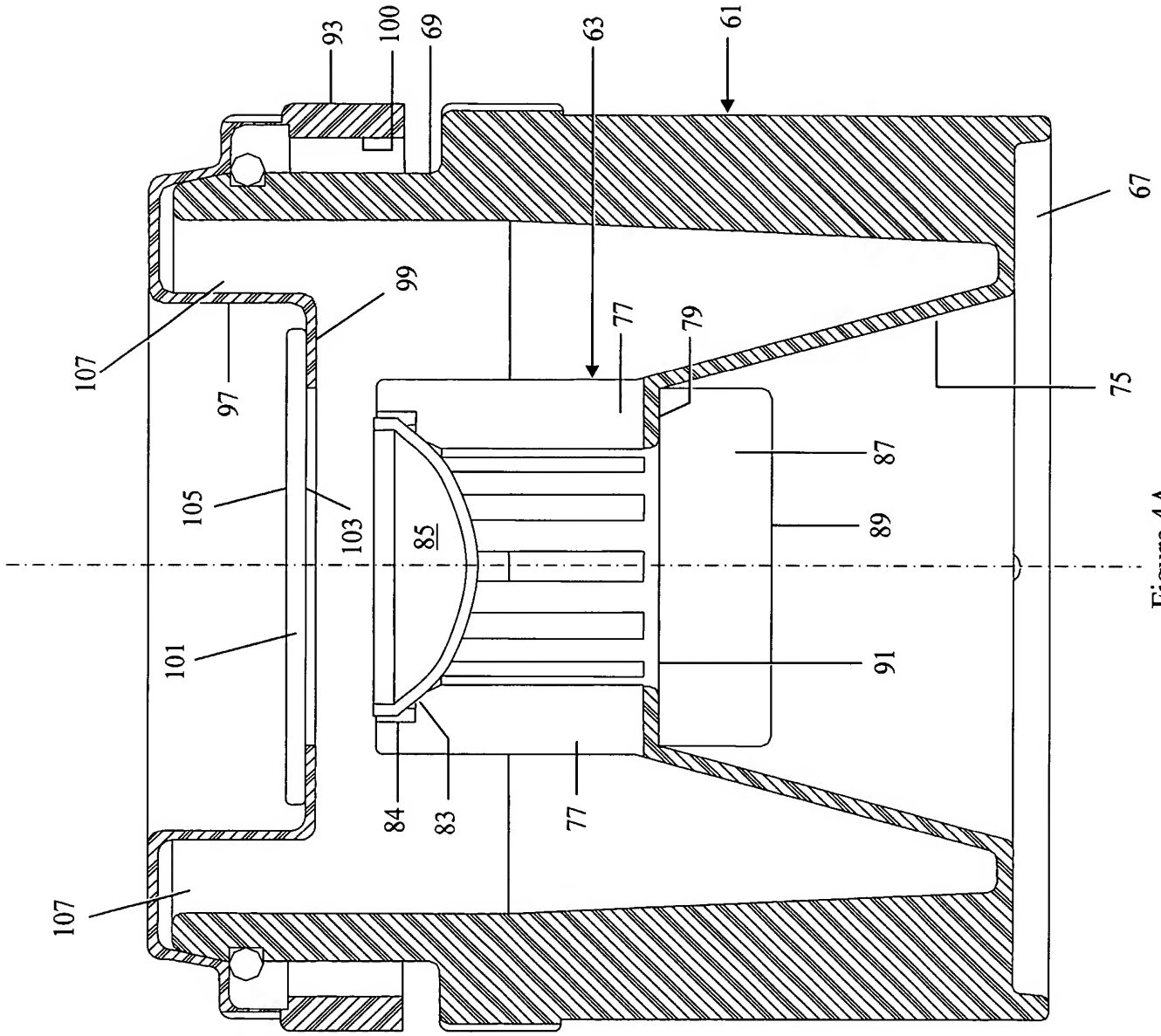
107
107
105
65
93
103
101
100
81
15¹
74
71
73
85
84
69
83
63
77
77
79
61
89
91
87
75
67

Figure 4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100
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103
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89
101
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84
83
77
107

Figure 4A

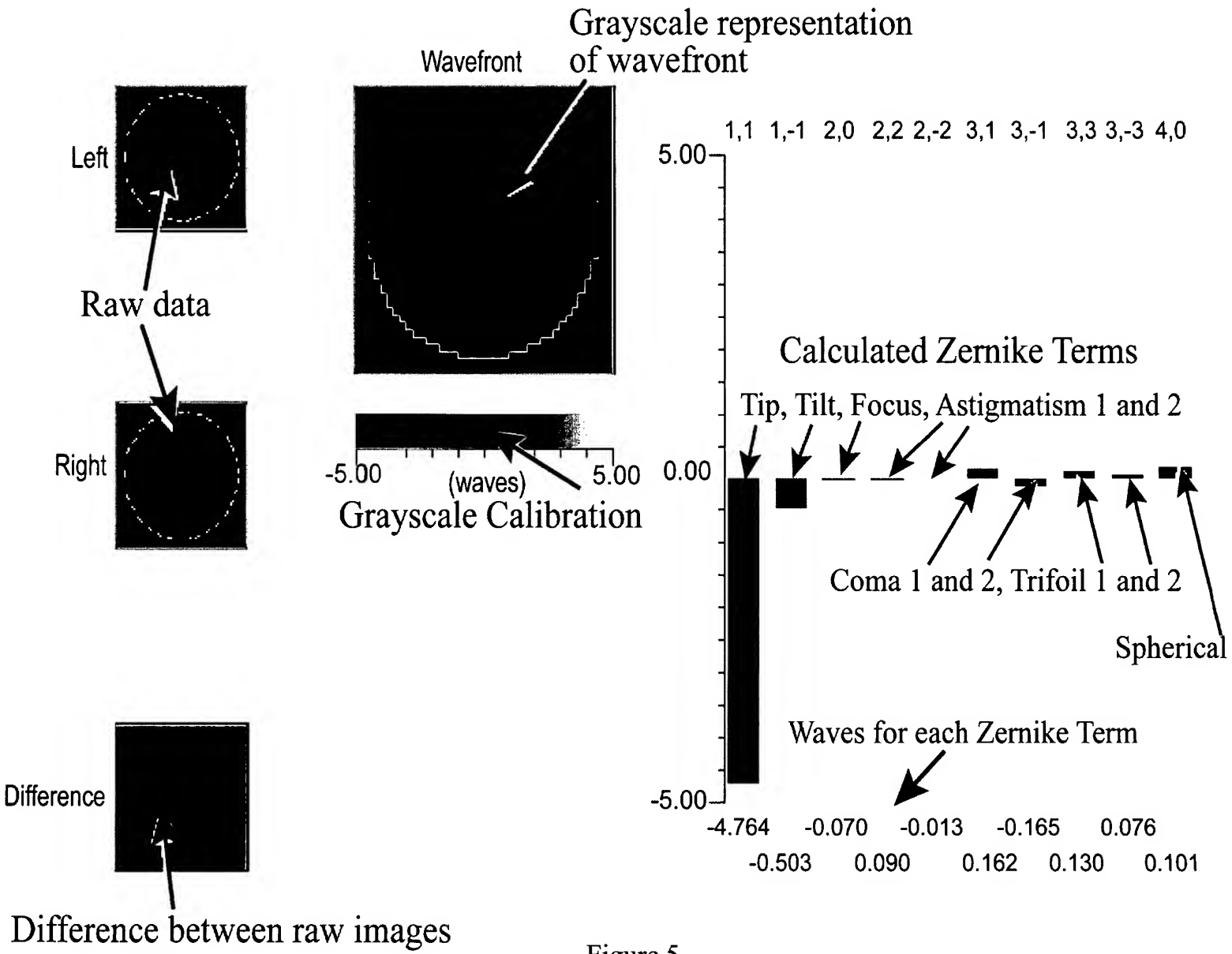

Grayscale representation of wavefront
Wavefront
Left
Raw data
Right
Difference
Difference between raw images
-5.00
(waves)
5.00
Grayscale Calibration
1,1 1,-1 2,0 2,2 2,-2 3,1 3,-1 3,3 3,-3 4,0
5.00
0.00
-5.00
Calculated Zernike Terms
Tip, Tilt, Focus, Astigmatism 1 and 2
Coma 1 and 2, Trifoil 1 and 2
Spherical
Waves for each Zernike Term
-4.764 -0.070 -0.013 -0.165 0.076
-0.503 0.090 0.162 0.130 0.101

Figure 5

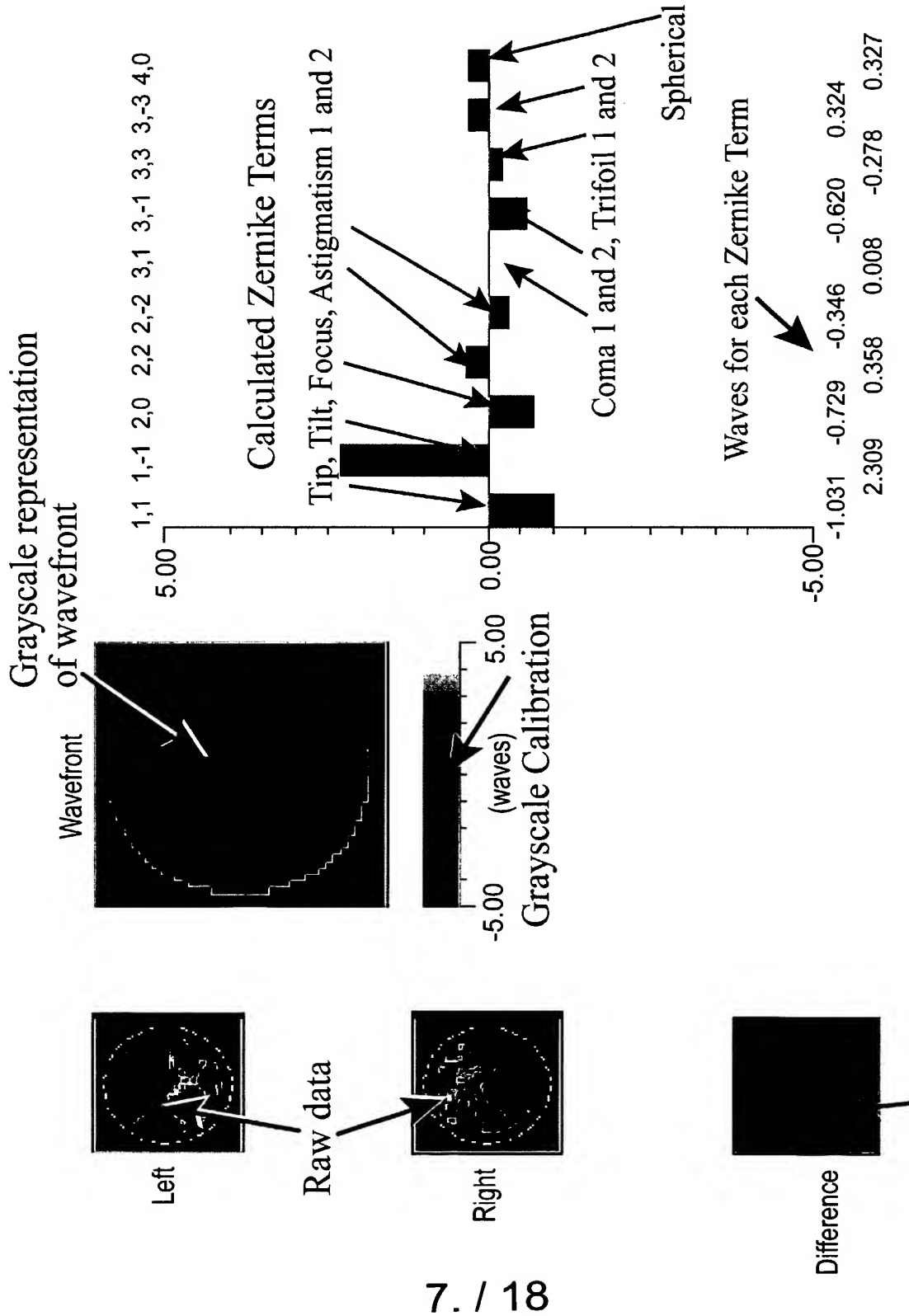

Grayscale representation of wavefront
Wavefront
Grayscale Calibration
5.00
(waves)
-5.00
Calculated Zernike Terms
1,1 1,-1 2,0 2,2 2,-2 3,1 3,-1 3,3 3,-3 4,0
5.00
0.00
-5.00
Tip, Tilt, Focus, Astigmatism 1 and 2
Coma 1 and 2, Trifoil 1 and 2
Spherical
Waves for each Zernike Term
-1.031 -0.729 0.358 2.309
-0.346 0.008
-0.620 -0.278
0.324 0.327
Left
Raw data
Right
Difference
Difference between raw images

Figure 6

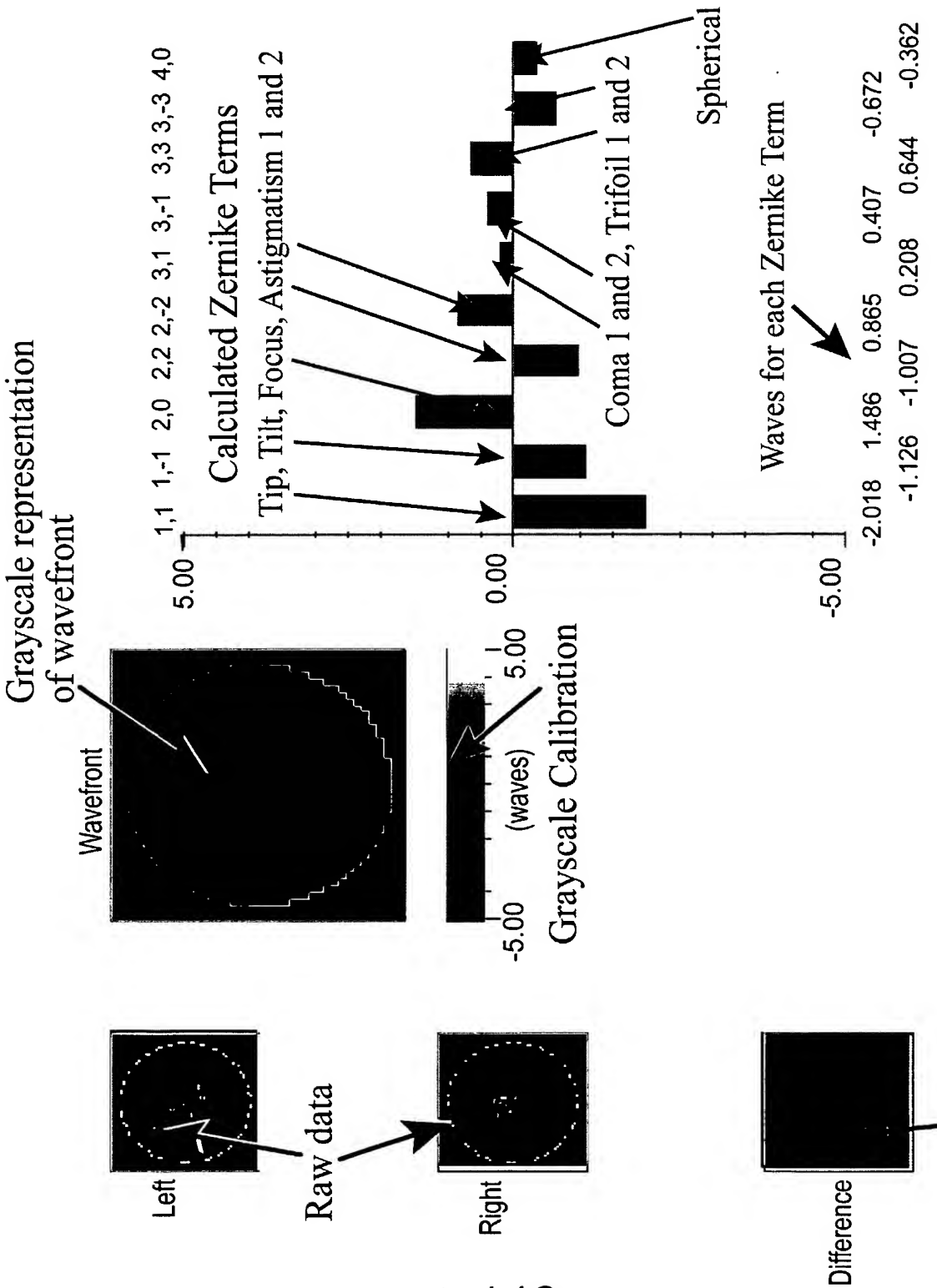

Grayscale representation of wavefront
Wavefront
Grayscale Calibration
5.00
(waves)
-5.00
Calculated Zernike Terms
1,1 1,-1 2,0 2,2 2,-2 3,1 3,-1 3,3 3,-3 4,0
Tip, Tilt, Focus, Astigmatism 1 and 2
Coma 1 and 2, Trifoil 1 and 2
Spherical
Waves for each Zernike Term
5.00
0.00
-5.00
-2.018 1.486 0.865 0.407 -0.672
-1.126 -1.007 0.208 0.644 -0.362
Left
Raw data
Right
Difference
Difference between raw images

Figure 7

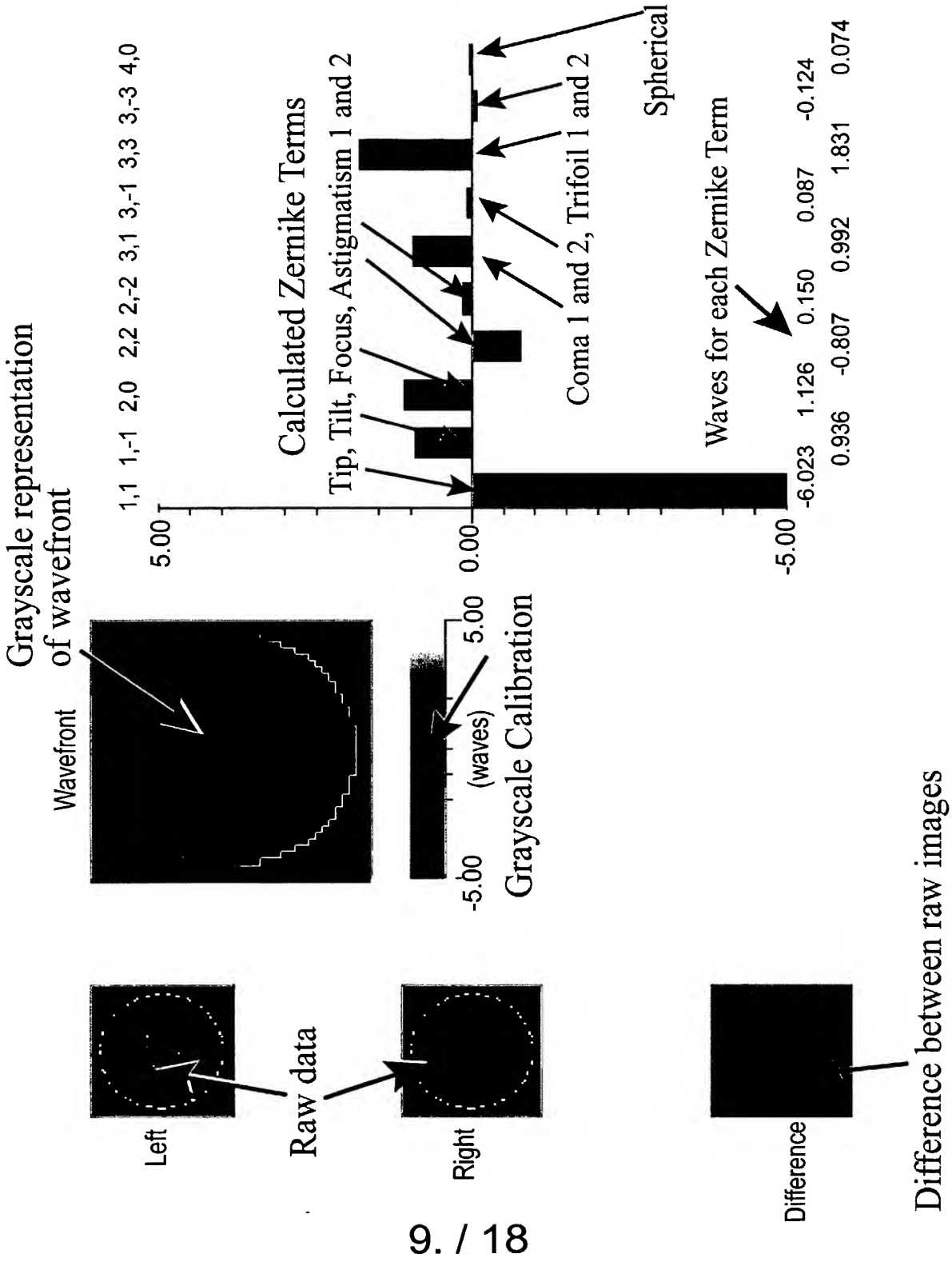

Grayscale representation of wavefront
Wavefront
Calculated Zernike Terms
Tip, Tilt, Focus, Astigmatism 1 and 2
Coma 1 and 2, Trifoil 1 and 2
Spherical
1,1 1,-1 2,0 2,2 2,-2 3,1 3,-1 3,3 3,-3 4,0
5.00
0.00
-5.00
Waves for each Zernike Term
-6.023 1.126 0.150 0.087 -0.124
0.936 -0.807 0.992 1.831 0.074
5.00
-5.00
(waves)
Grayscale Calibration
Left
Raw data
Right
Difference
Difference between raw images

Figure 8

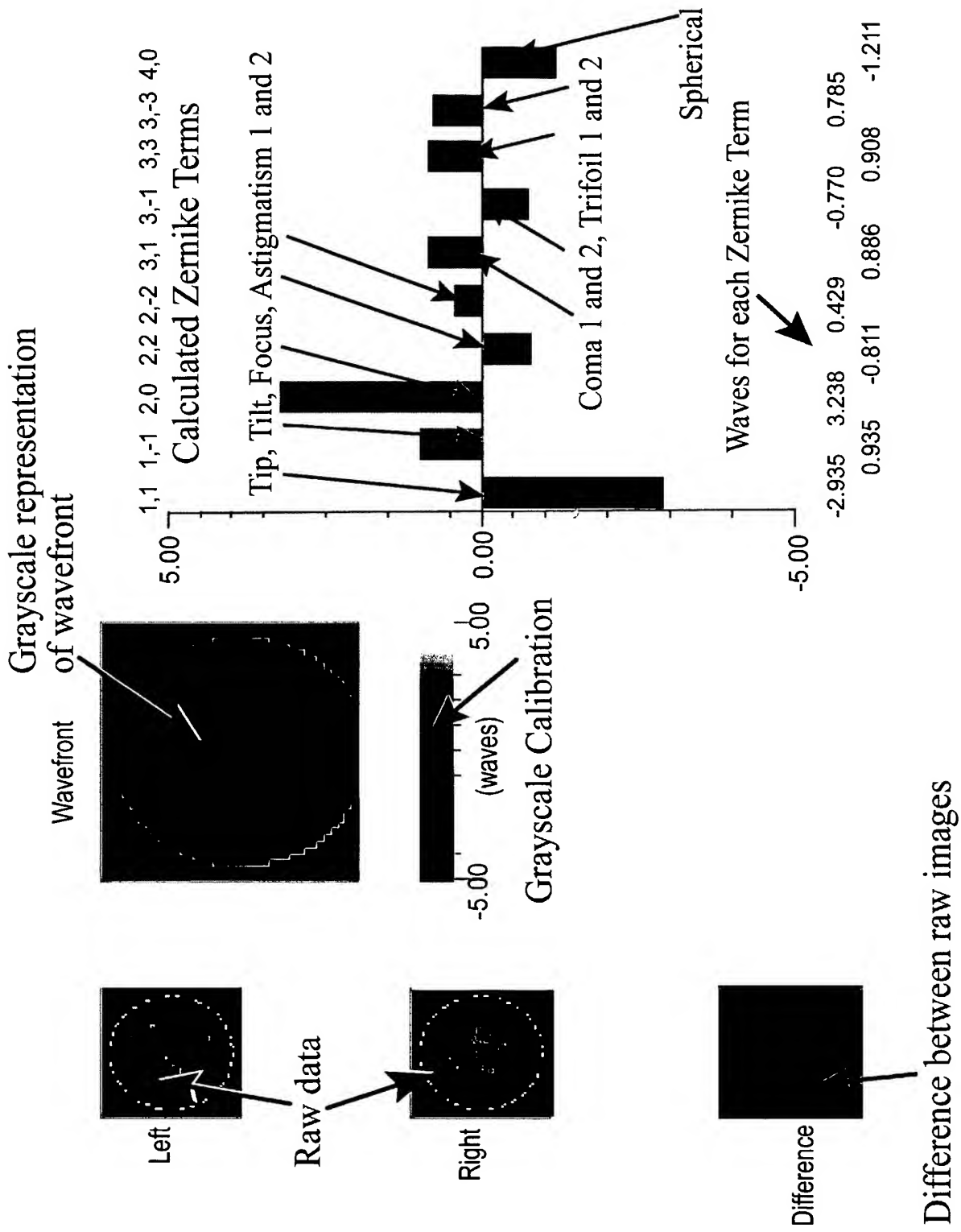
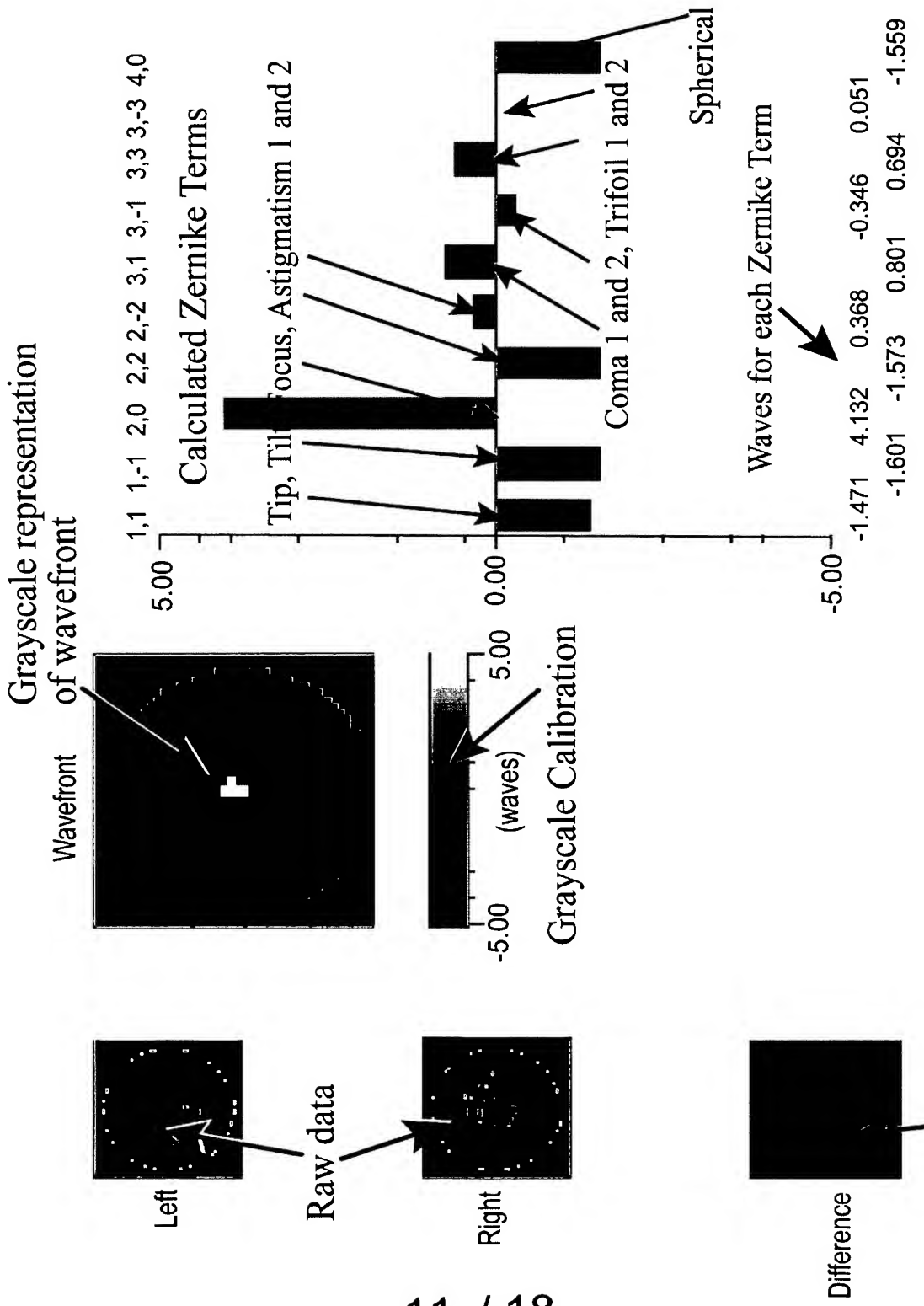

Grayscale representation of wavefront
Wavefront
Calculated Zernike Terms
1,1 1,-1 2,0 2,2 2,-2 3,1 3,-1 3,3 3,-3 4,0
5.00
0.00
-5.00
Tip, Tilt, Focus, Astigmatism 1 and 2
Coma 1 and 2, Trifoil 1 and 2
Spherical
Waves for each Zernike Term
-2.935 3.238 0.429 -0.770 0.785
0.935 -0.811 0.886 0.908 -1.211
5.00
-5.00
(waves)
Grayscale Calibration
Left
Raw data
Right
Difference
Difference between raw images

Figure 9



11. / 18

Figure 10

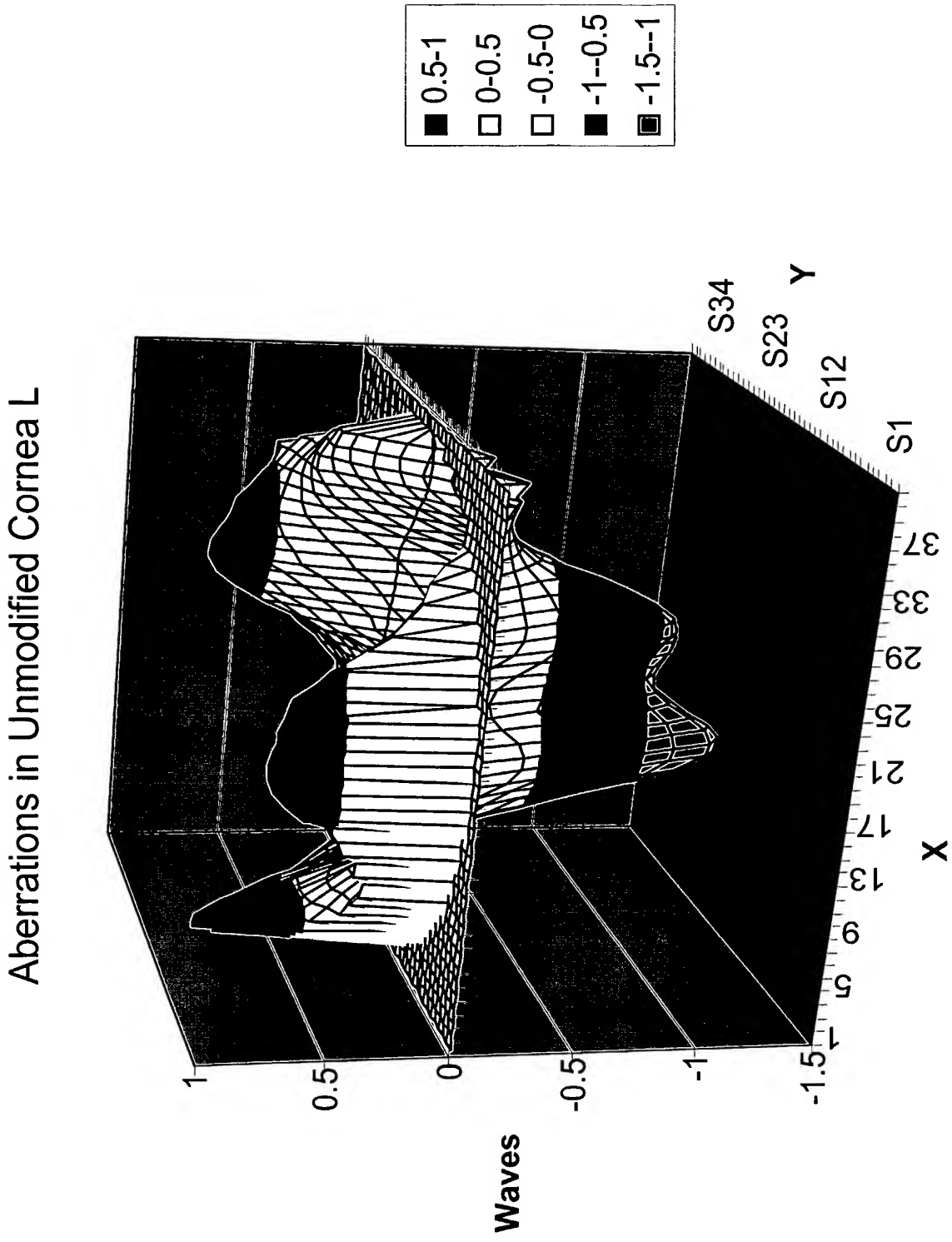

Aberrations in Unmodified Cornea L
0.5-1
0-0.5
-0.5-0
-1--0.5
-1.5--1
Waves
1
0.5
0
-0.5
-1
-1.5
X
1
5
9
13
17
21
25
29
33
37
Y
S1
S12
S23
S34

Figure 11

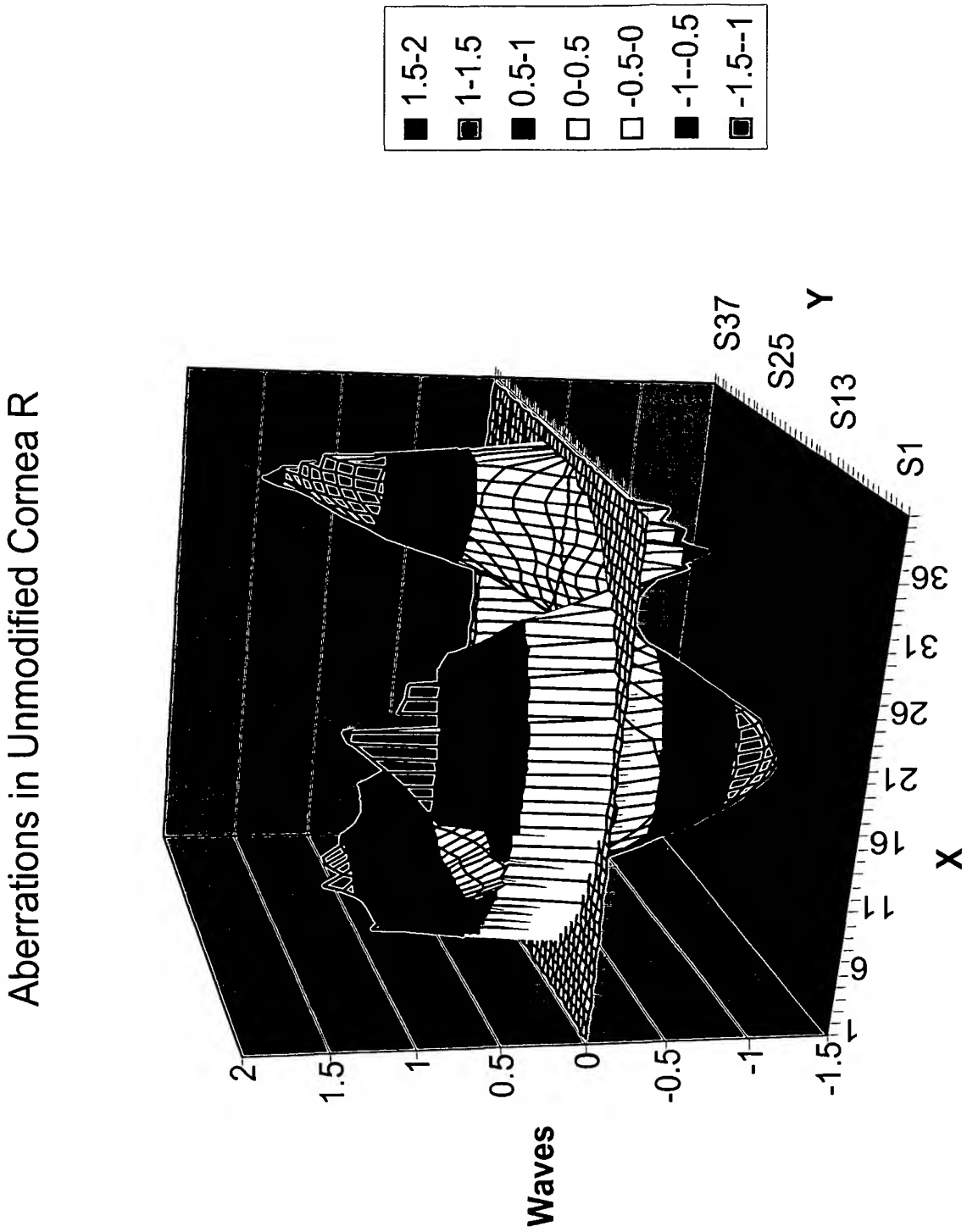
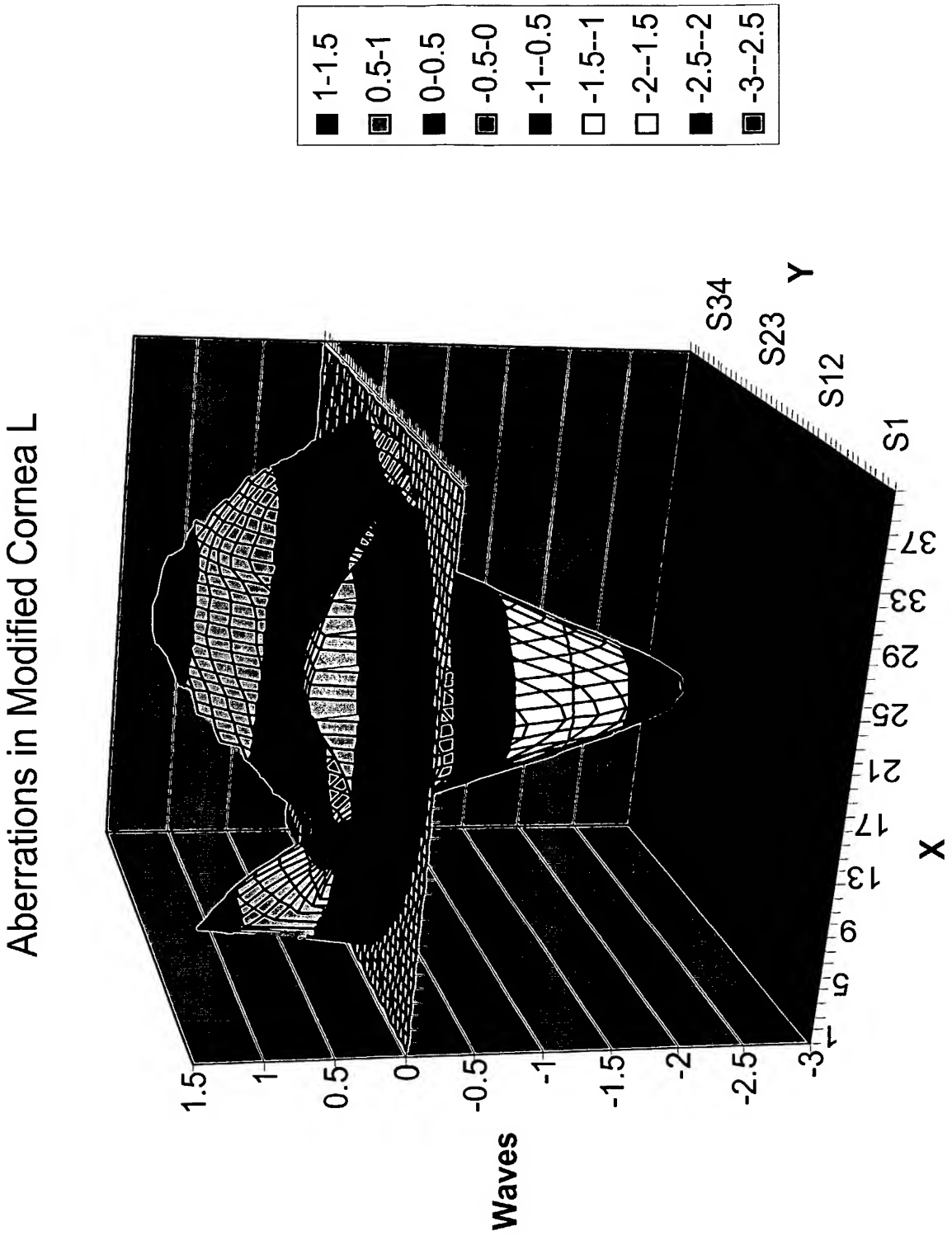

Aberrations in Unmodified Cornea R
1.5-2
1-1.5
0.5-1
0-0.5
-0.5-0
-1--0.5
-1.5--1
Waves
2
1.5
1
0.5
0
-0.5
-1
-1.5
X
1
6
11
16
21
26
31
36
Y
S1
S13
S25
S37

Figure 12


Aberrations in Modified Cornea L
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0.5-1
0-0.5
-0.5-0
-1--0.5
-1.5--1
-2--1.5
-2.5--2
-3--2.5
Waves
1.5
1
0.5
0
-0.5
-1
-1.5
-2
-2.5
-3
X
1
5
9
13
17
21
25
29
33
37
Y
S1
S12
S23
S34

Figure 13

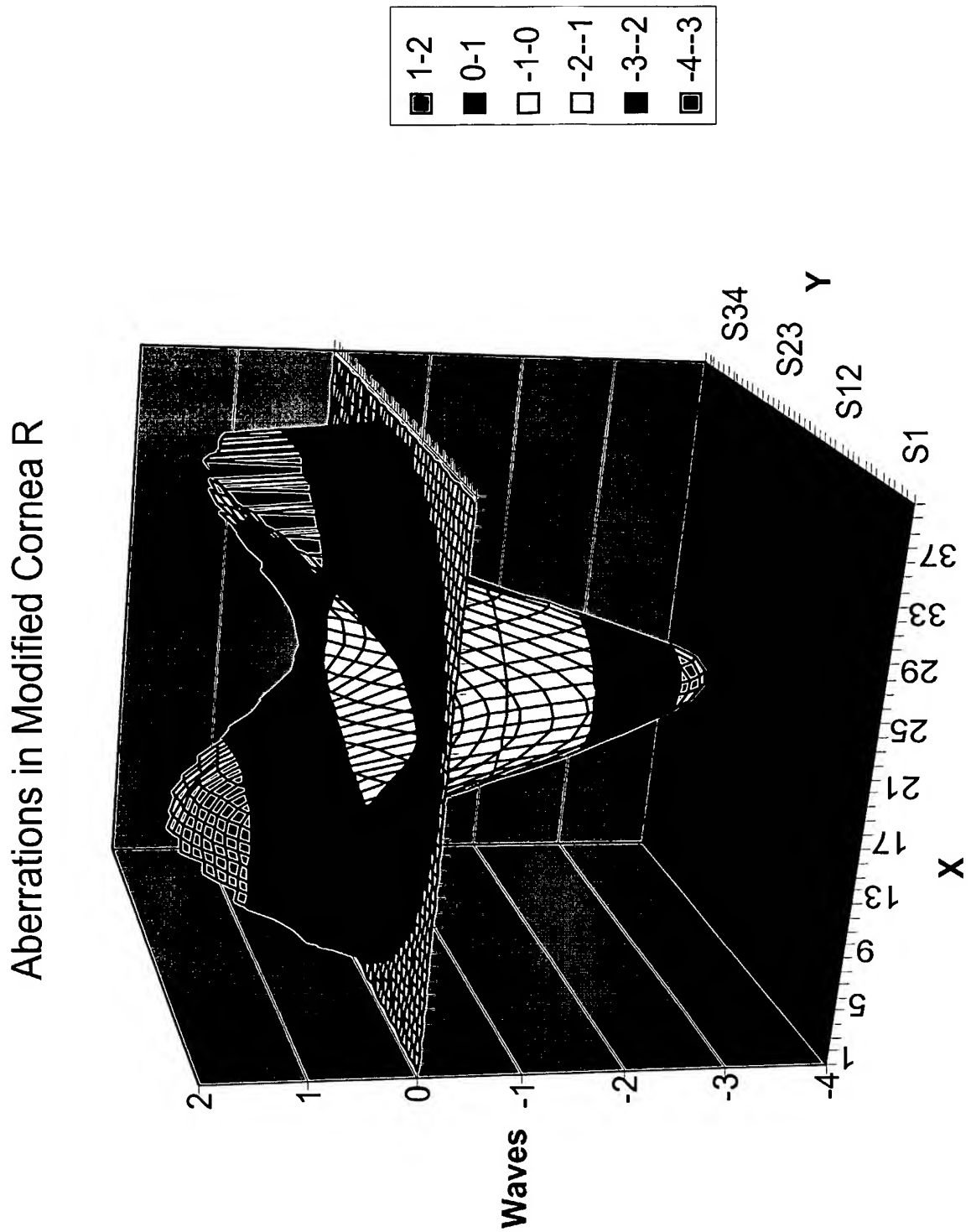
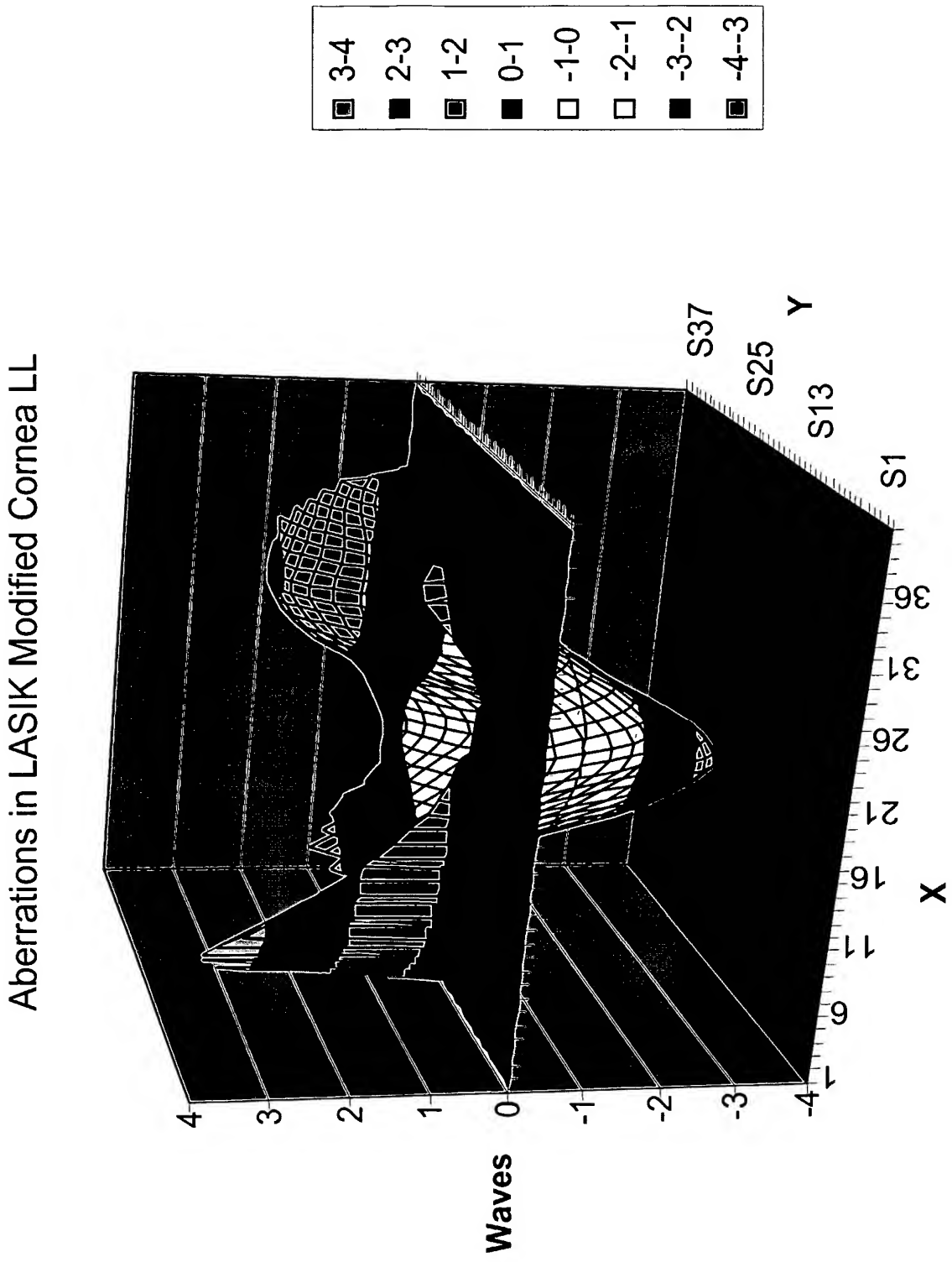

Aberrations in Modified Cornea R
1-2
0-1
-1-0
-2--1
-3--2
-4--3
Waves
2
1
0
-1
-2
-3
-4
X
1
5
9
13
17
21
25
29
33
37
Y
S1
S12
S23
S34

Figure 14


Aberrations in LASIK Modified Cornea LL
3-4
2-3
1-2
0-1
-1-0
-2--1
-3--2
-4--3
Waves
4
3
2
1
0
-1
-2
-3
-4
X
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6
11
16
21
26
31
36
Y
S1
S13
S25
S37

Figure 15

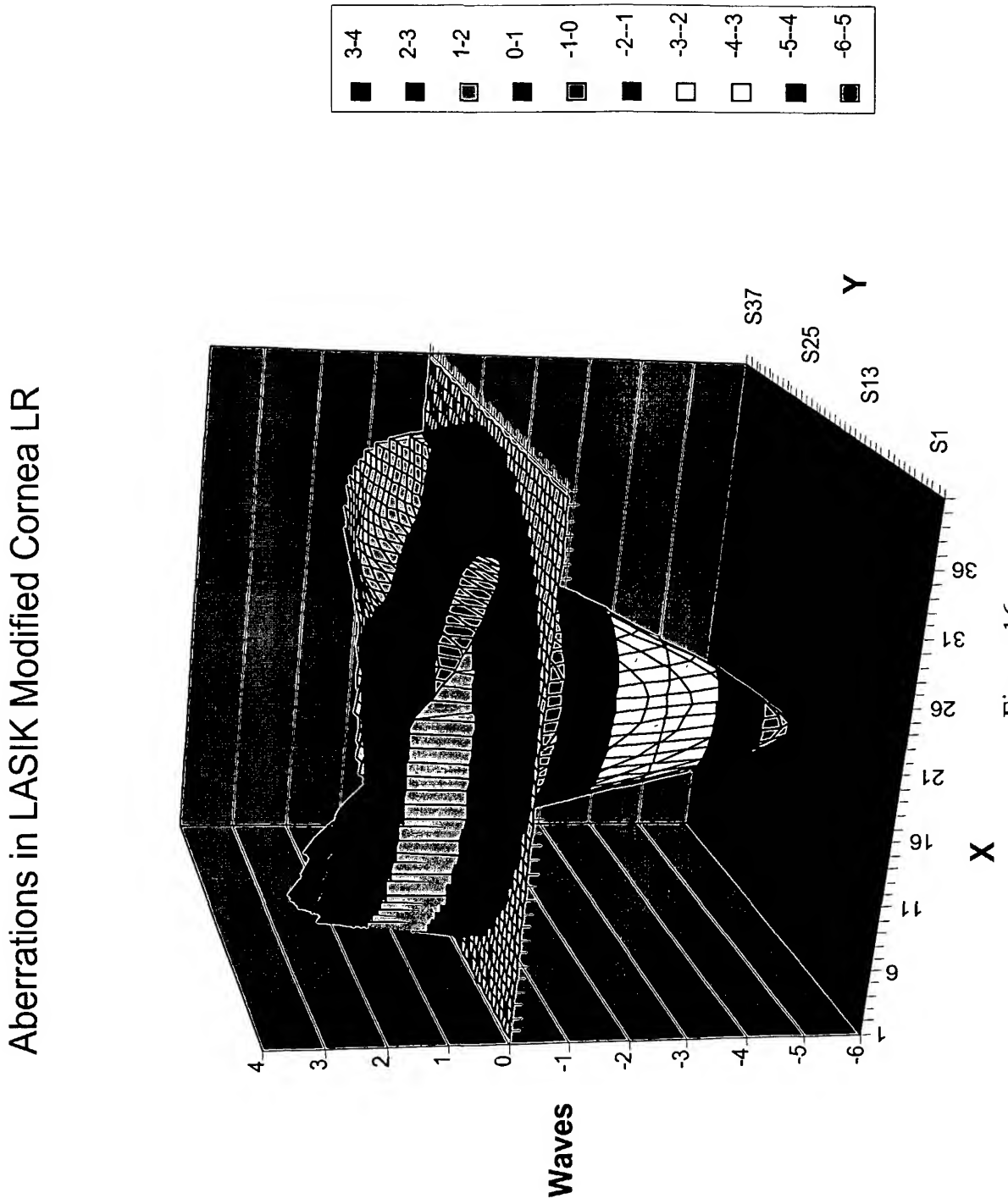
Aberrations in LASIK Modified Cornea LR
3-4
2-3
1-2
0-1
-1-0
-2--1
-3--2
-4--3
-5--4
-6--5
Waves
4
3
2
1
0
-1
-2
-3
-4
-5
-6
X
1
6
11
16
21
26
31
36
Y
S1
S13
S25
S37

Figure 16

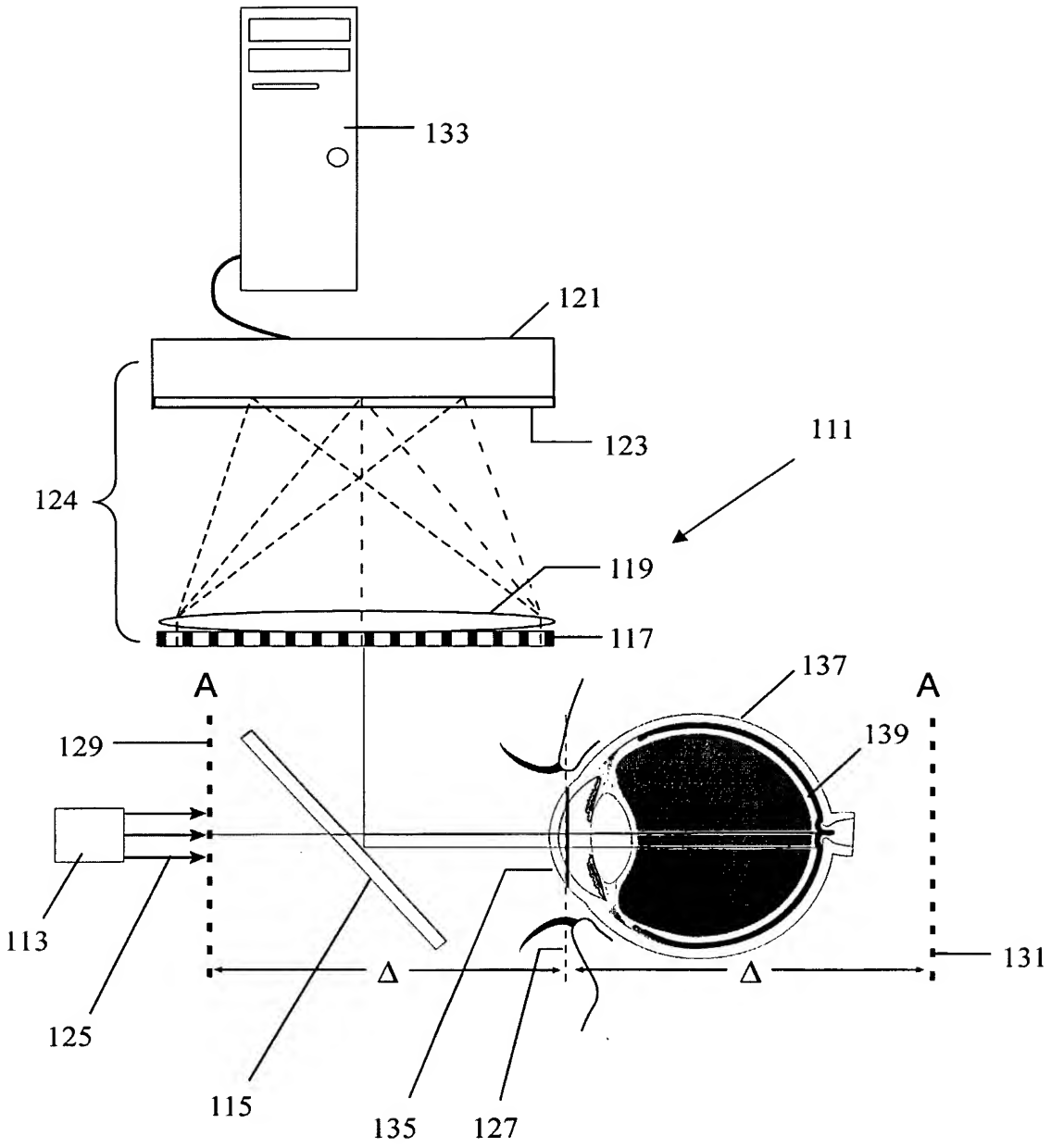
133
121
123
111
124
119
117
A
A
137
129
139
113
131
Δ
Δ
125
115
135
127

Figure 17

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/19912

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : A61B 3/10
US CL : 351/216
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 351/205, 206, 212, 216, 217, 218, 245, 246, 247; 422/102; 623/5.11, 5.12, 5.14, 5.16; 435/304.1; 206/5.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EAST and WEST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	US 6,286,959 B1 (OTTEN) 11 September 2001, see entire document.	1-6

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 August 2002 (11.08.2002)	19 DEC 2002
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer George Manuel Telephone No. (703) 308-0858

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/19912

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.